

Attorney Docket No.: 6056-236 (35926-136495)
AMENDMENT AND REPLY UNDER 37 C.F.R. § 1.111

IN THE CLAIMS

1. (Currently Amended) A substantially purified EC-3 protein isolated from ~~E.~~
carinatus Echis carinatus venom, characterized by:

(a) an apparent molecular mass of about 14,762 Da, as determined by
electrospray ionization mass spectrometry;

(b) elution from a C-18 ~~HPLC~~ high performance liquid
chromatography column at about 40% acetonitrile; and

(c) the ability to inhibit adhesion of Jurkat cells to ~~VCAM-1~~ vascular
cell adhesion molecule-1.

2. (Currently Amended) A substantially purified EC-3A peptide isolated from EC-3
protein which has been reduced and alkylated, characterized by:

(a) a molecular mass of about 8478 Da in its ethylpyridylated form, as
determined by electrospray ionization mass spectrometry;

(b) elution from a C-18 ~~HPLC~~ high performance liquid
chromatography column at about 42% acetonitrile; and

(c) the ability to inhibit adhesion of K562 cells to fibronectin.

3. (Currently Amended) A substantially purified EC-3B peptide isolated from EC-3
protein which has been reduced and alkylated with vinylpyridine, characterized by:

(a) a molecular mass of about 7950 Da in its carboxymethylated form,
as determined by electrospray ionization mass spectrometry;

(b) elution from a C-18 ~~HPLC~~ high performance liquid
chromatography column at about 46% acetonitrile; and

Attorney Docket No.: 6056-236 (35926-136495)
AMENDMENT AND REPLY UNDER 37 C.F.R. § 1.111

(c) the ability to inhibit adhesion of Jurkat cells to ~~VCAM-1~~ vascular cell adhesion molecule-1.

4. (Currently Amended) ~~A~~ The substantially purified EC-3A peptide of Claim 2 comprising the a sequence represented by SEQ ID NO:19 or a biologically active fragment or derivative thereof.

5. (Currently Amended) The substantially purified EC-3A peptide of Claim 4-2 comprising the a sequence represented by SEQ ID NO:2.

6. (Currently Amended) ~~A~~ The substantially purified EC-3B peptide of Claim 3 comprising the a sequence represented by SEQ ID NO:20, or a biologically active fragment or derivative thereof.

7. (Currently Amended) The substantially purified EC-3B peptide of Claim 3 The peptide of claim 6 comprising a the sequence represented by SEQ ID NO:3.

8. (Currently Amended) ~~A~~ The substantially purified EC-3 protein of Claim 1 comprising two subunits, wherein one subunit comprises the sequence SEQ ID NO:19 or a biologically active fragment or derivative thereof and one subunit comprises the sequence SEQ ID NO:20 or a biologically active fragment or derivative thereof.

9. (Currently Amended) ~~A biologically active fragment according to claim 6 having the sequence~~ The substantially purified EC-3B peptide of Claim 6, wherein the biologically active fragment comprises a peptide represented by an amino acid sequence X-Y-Met-Leu-Asp-Z, where X is H or a blocking group, Y is zero or more amino acids, and Z is OH or zero or more amino acids.

10. (Currently Amended) ~~A biologically active fragment according to claim 9 wherein said fragment is~~ The substantially purified EC-3B peptide of Claim 9, wherein the biologically active fragment comprises a peptide having from about 3 to about 20 amino acids.

Attorney Docket No.: 6056-236 (35926-136495)
AMENDMENT AND REPLY UNDER 37 C.F.R. § 1.111

11. (Currently Amended) ~~A fragment according to claim 10 having the sequence SEQ ID NO: 16~~ The substantially purified EC-3B peptide of Claim 9, wherein the biologically active fragment is represented by SEQ ID No: 16.

12. (Currently Amended) ~~A fragment according to claim 10 having the sequence SEQ ID NO: 14.~~ The substantially purified EC-3B peptide of Claim 9, wherein the biologically active fragment is represented by SEQ ID No: 14.

13. (Withdrawn)

14. (Withdrawn)

15. (Withdrawn)

16. (Withdrawn)

17. (Withdrawn)

18. (Withdrawn)

19. (Withdrawn)

20. (Currently Amended) A substantially purified ~~eichistatin~~ echistatin polypeptide represented by SEQ ID NO: 9, in which the Arg-Gly-Asp residues at positions 24-26 are replaced by Met-Leu-Asp, ~~or a biologically active fragment or derivative thereof.~~

21. (Currently Amended) A method of isolating a peptide from a venom, wherein the peptide that binds to an integrin of interest, from venom comprising:

- (a) dissolving venom in a solvent,
- (b) centrifuging the dissolved venom to remove high molecular weight proteins,
- (c) fractionating the supernatant from step (b),

Attorney Docket No.: 6056-236 (35926-136495)
AMENDMENT AND REPLY UNDER 37 C.F.R. § 1.111

- (d) immobilizing the fractions from step (c) on a solid support,
- (e) adding detectably labeled cells that express the integrin of interest to the immobilized fractions,
- (f) detecting the number of cells bound to each immobilized fraction, and
- (g) isolating peptide from those fractions which showed enhanced cell binding in step (f).

22. (Original) A composition comprising a pharmaceutically acceptable carrier and the protein or peptide of any of claims 1-12, or a pharmaceutically acceptable salt thereof.

23. (Withdrawn)

24. (Original) A method of inhibiting the binding of an $\alpha 4$ integrin to VCAM-1 comprising contacting a cell that expresses the $\alpha 4$ integrin with an effective amount of a protein or peptide according to one of claims 1-12, or a pharmaceutically acceptable salt thereof.

25. (Original) The method of claim 24 wherein the integrin is $\alpha 4\beta 1$ or $\alpha 4\beta 7$.

26. (Original) A method of inhibiting the binding of a $\alpha 4\beta 7$ integrin to MadCAM-1 comprising contacting a cell that expresses $\alpha 4\beta 7$ with an effective amount of a protein or peptide according to one of claims 1-12, or a pharmaceutically acceptable salt thereof.

27. (Original) A method of inhibiting the binding of an $\alpha 4$ integrin to CS-1 comprising contacting a cell that expresses the $\alpha 4$ integrin with an effective amount of a protein or peptide according to one of claims 1-12, or a pharmaceutically acceptable salt thereof.

28. (Original) A method of inhibiting the interaction between cells expressing an $\alpha 4$ integrin and VCAM-1 in a patient in need of such treatment comprising administration of a therapeutically effective amount of a composition according to claim 22.

Attorney Docket No.: 6056-236 (35926-136495)
AMENDMENT AND REPLY UNDER 37 C.F.R. § 1.111

29. (Original) A method of inhibiting the interaction between cells expressing an $\alpha 4$ integrin and MadCAM-1 in a patient in need of such treatment comprising administration of a therapeutically effective amount of a composition according to claim 22.

30. (Original) A method of inhibiting the interaction between cells expressing an $\alpha 4$ integrin and CS-1 in a patient in need of such treatment comprising administration of a therapeutically effective amount of a composition according to claim 22.

31. (Original) A substantially purified EC-3A peptide characterized by:

- (a) a sequence having substantial homology with SEQ ID NO:2; and
- (b) the ability to inhibit adhesion of K562 cells to fibronectin.

32. (Original) A substantially purified EC-3B peptide characterized by:

- (a) a sequence having substantial homology with SEQ ID NO:3; and
- (b) the ability to inhibit adhesion of Jurkat cells to VCAM-1.

33. (Withdrawn)